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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/537,824	02/08/2006	Marcello Allegretti	3765-0115PUS1	8576

2292 7590 11/08/2007

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EXAMINER	
LOEWE, SUN JAE Y	
ART UNIT	PAPER NUMBER
1626	

NOTIFICATION DATE	DELIVERY MODE
11/08/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

mailroom@bskb.com

Office Action Summary	Application No.	Applicant(s)	
	10/537,824	ALLEGRETTI ET AL.	
	Examiner	Art Unit	
	Sun Jae Y. Loewe	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 October 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6 and 8* is/are pending in the application.

4a) Of the above claim(s) *4* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,5,6 and 8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/8/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-6 and 8 are pending in the instant application. Claim 7 was cancelled by preliminary amendment filed on June 8, 2005.

Election/Restrictions

2. Applicant's election with traverse of Group I, and "(R)(-)-3-[(4'-isobutyl)phenyl]butan-2-one." (claims 1-3, 5, 6 and 8), in the response filed on October 1, 2007 is acknowledged. The traverse is on the ground(s):

a) " First, Applicants point out that unity of invention was found for this application during the International stage of the PCT process. An International application which complies with PCT unity of invention requirements must then be accepted by all of the designated and elected offices, including the U.S. Patent and Trademark Office (USPTO) since Article 27(1) of the Patent Cooperation Treaty does not permit any national law or national office to require compliance with different regulations relating to the contents of the International application. "

The Applicant is reminded that Article 27(1) of the Patent Cooperation Treaty applies to the requirements for the *form* and *contents* of the international application, not to the Unity of Invention practice. The propriety of requiring restriction in a national stage application is governed by MPEP § 1850 and the PCT rules referred to therein.

b) " In addition, the claims have a single inventive concept in that all of the compounds have a very similar technical structure and possess the same property of inhibiting IL-8 induced human PMNs chemotaxis. "

MPEP § 1850.III.B defines the criteria for Markush alternatives to fulfill the "special technical feature" requirement under PCT Rule 13.2. Criteria (B)(1) requires that a significant structural element is *shared by all of the alternatives*. Thus, the fact that all the compounds to have *"very similar"* technical feature is not sufficient to comply with PCT Rule 13.2.

The restriction requirement dated July 31, 2007 is still deemed to be proper and is therefore made FINAL.

3. MPEP § 803.02 provides guidelines for election of species in Markush-type claims. These guidelines were followed for the search and examination detailed herein.

The elected species (the claimed process of using "(R)(-)-3-[(4'-isobutyl)phenyl]butan-2-one.") was not allowable (MPEP § 803.02), thus Markush-type claims were rejected and the subject matter drawn to nonelected species held withdrawn from further consideration. Claims 1-3, 5, 6 and 8 were further examined to the extent necessary to determine patentability. The *search* was *limited* to the elected species.

It has been determined that the entire scope claimed is not patentable.

4. Claim 4 withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected subject matter.

Information Disclosure Statement

5. The information disclosure statement (IDS) submitted on June 8, 2005 was in compliance with the provisions of 37 CFR 1.97 and 37 CFR 1.98. The IDS was considered. A signed copy of form 1449 is enclosed herewith.

Claim Objections

6. Claims 1-3, 5, 6 and 8 objected to for containing non-elected subject matter.

7. Claim 7 objected to because of the following informality. The claim is drawn to "The method ... further comprising a pharmaceutically acceptable carrier". It is suggested that the wording be modified such that the composition used in the method, rather than the method itself, further comprises a pharmaceutically acceptable carrier.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 1-3, 5, 6 and 8 rejected under 35 U.S.C. 112, first paragraph. The specification is enabling for making and using compounds reduced to practice (ie. species of claim 3) for the treatment of ischemia and reperfusion (see Allegretti et al., page 4322, 2nd column, 1st paragraph). The specification is not enabling for

a) Using compounds within the Markush claim that are not supported by the disclosure (ie. species not reduced to practice).

b) Method of treating diseases other than ischemia and reperfusion; method of preventing any of the claimed disease

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with the claims.

The standard for determining whether the specification meets the enablement requirement was cast in the Supreme Court decision of *Mineral Separation v. Hyde*, 242 U.S. 261, 270 (1916) which postured the question: is the experimentation needed to practice the invention undue or unreasonable? That standard is still the one to be applied. *In re Wands*, 858 F.2d 731, 737, 8USPQ2s 1400, 1404 (Fed. Cir. 1988). MPEP 2164.01(a) states "There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is undue". The factors are applied below to the instant claims.

The breadth of the claims

a) Claims drawn to compounds not reduced to practice.

b) Claims drawn to the method of treating/preventing diseases mediated by IL 8 (eg. inflammatory diseases such as rheumatoid arthritis, asthma).

The nature of the invention

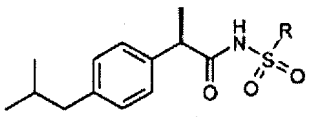
a) The compounds are disclosed to be IL8 inhibitors.

b) The claims to the treatment/prevention of diseases is based on the ability of the compounds to inhibit IL 8.

The state of the prior art/level of ordinary skill/level of predictability

a) The level of ordinary skill is high, but the level of predictability in the art is low. Although SAR studies are not available for the instantly claimed Markush group of compounds, these studies have been disclosed for other compounds that IL8 inhibitors, see example below.

- Allegretti et al., Table 3:



– For example, changing R from methyl to trifluoromethyl results in at least a 100-fold decrease in % inhibition

In view of a disclosed absence of structure-activity correlation, is not known what structural limitations are required for preservation of activity within the Markush formula claimed. Further, as evidenced by the example above, it is recognized in the art that the level of predictability is low for inhibiting IL 8. Thus, one of ordinary skill would not be able to predict that the compounds embraced by the claims are active inhibitors of IL 8.

b) An art recognized relationship exists between IL 8 inhibition and treatment of ischemia/reperfusion, based on in vivo animal models (Allegretti et al., page 4322, 2nd column, first paragraph). However, an art recognized relationship does not exist between IL 8 inhibition and the treatment of any other disease within the scope of the claims (ie. diseases that involve IL 8 etiology).

Moreover, the level of predictability for treating diseases whose etiology involves IL 8 is low. See illustrative points below:

- In clinical trials targeting the treatment of rheumatoid arthritis using TNF-α inhibition, 30% of individuals failed to respond (McCulloch et al., p. 865, 2nd column, 1st paragraph).
- Multiple mediators are involved in inflammatory conditions such as asthma. Due to the redundancy of the mediator effects, it is unlikely that targeting a single mediator will produce a major clinical benefit (Barnes, p. 541, 1st column, 3rd paragraph; McCulloch et al., p. 865, 2nd column, 1st paragraph).

The amount of direction provided by the inventor/existence of working examples

a) Direction and working examples are limited to the compounds reduced to practice.

b) No direction/working examples.

The quantity of experimentation needed to make or use the invention

a) It is not known which of the unrepresented compounds meet the structural requirements for activity. Thus, one of ordinary skill would not be enabled by the disclosure to make/use the claimed IL 8 inhibitors. The amount of experimentation needed to practice the invention is deemed to be undue. Further, absent a utility alternate to IL 8 inhibition, one of ordinary skill would not be enabled to use the compounds that are not adequately supported in the disclosure.

b) Absent guidance and/or art recognized correlation between IL 8 inhibition and treatment of the diseases claimed, particularly in view of the unpredictability in the art, one of ordinary skill is not enabled to practice the claimed invention. The amount of experimentation is undue.

Conclusion

9. No claims allowed.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sun Jae Y. Loewe whose telephone number is (571) 272-9074. The examiner can normally be reached on M-F 7:30-5:00 Est.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph McKane can be reached on (571)272-0699. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Sun Jae Y. Loewe
Art Unit 1626

REBECCA ANDERSON
PRIMARY EXAMINER